Lifestyle behaviours and health measures of women at increased risk of breast cancer taking chemoprevention

Running title: Lifestyle of women at increased breast cancer risk

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Abstract

Background

Women at increased risk of breast cancer are eligible for chemoprevention. Healthy lifestyles are potentially important for these women in terms of improving the efficacy, minimising side effects of chemopreventative agents and reducing risk of breast cancer and other lifestyle related conditions.

Methods

We examined lifestyle risk factors and health measures in 136 premenopausal women taking tamoxifen for prevention of breast cancer (Tam-Prev study) compared to an age-matched female population from the Health Survey for England 2012.

Results

The Tam-Prev population had high rates of overweight and obesity (59.2%) and low adherence to physical activity recommendations (30.6%) which were comparable to the general population (respectively 55.2% and 35.1%). Fewer Tam-Prev participants were current smokers (10.5% vs. 18.2%, p=0.032), but more exceeded UK alcohol recommendations (45.0% vs. 18.7%, p<0.001). Tam-Prev participants had suboptimal diets; proportions not meeting fibre, saturated fat and non-milk extrinsic sugar recommendations were 87.8%, 64.9% and 21.4% respectively. Many Tam-Prev participants had markers of cardiovascular disease and the metabolic syndrome. Health behaviours did not change during the first year on tamoxifen.

Conclusion

Tam-Prev participants had a high prevalence of unhealthy lifestyle behaviours and health measures, similar to an age-matched English cohort. Improving these measures in women at increased breast cancer risk could significantly decrease rates of breast cancer and other non-communicable diseases.

Registration: ISRCTN 53844391

Keywords:
Chemoprevention, lifestyle, diet, physical activity, weight, tamoxifen, breast cancer

Background

Breast cancer (BC) is the most common cancer in the UK with 55,122 diagnoses in 2015[1]. Expert reports estimate maintaining a healthy weight, limiting alcohol, and being physically active could prevent 19-38% of BC in the UK[2,3]. Further reductions would be achieved through not smoking[4,5].

Tamoxifen is one of three drugs licenced for chemoprevention of BC in women at increased risk of BC in the UK. Tamoxifen reduces BC risk by 40% but carries an increased risk of venous thromboembolism and postmenopausal endometrial cancer, as well as vasomotor side effects.

Although evidence is mixed, there are suggestions from the adjuvant[6] and prevention[7] settings that chemopreventative medications are less effective in overweight women, and carry more side effects[8–10]. Furthermore since the majority of women taking chemoprevention will not develop BC[11], they need to attend to their risk of other lifestyle-related diseases, for example cardiovascular disease (CVD).

There are no published data on the lifestyle behaviours of women taking BC chemoprevention. This paper describes the lifestyle behaviours and health measures of women on the Tamoxifen Prevention Study[12] (Tam-Prev, ISRCTN 53844391), and changes during a year of chemoprevention.

Materials and Methods

Participants

The Tam-Prev recruited 136 premenopausal women at increased risk of BC between 2011-2012 to establish uptake of tamoxifen for BC prevention, and to determine who is most likely to benefit.

The Tam-Prev study has been described previously[12]. Women were eligible if they were at moderately high or high risk of BC (≥17% lifetime risk)[13], attending a regional Family History Clinic (FHC), aged 33-46 years, premenopausal and not on hormonal contraception. From 1279 eligible women invited, 136 agreed to take tamoxifen for one year (10.6% uptake).

Procedures

Women were asked to take tamoxifen (20mg/d) and were reviewed at eight weeks and one year. No lifestyle advice was given. All participants had previously been given a leaflet on BC prevention upon joining the FHC which included advice to control weight, limit alcohol and increase physical activity (PA).

Assessments at baseline (before commencing tamoxifen) and one year included weight and body fat determined by multi-frequency bioelectrical impedance (MC-180MA; Tanita Europe, Amsterdam, The Netherlands), waist circumference, fasting lipids, insulin and glucose taken using standardised methods described previously[14]. Self-reported dietary intake was assessed at baseline and one year from seven day food diaries checked for completeness with the respondent and analysed using WISP v3.3 (Tinuviel Software, Anglesey, UK) for mean daily saturated fatty acids, fibre (Association of Official Analytical Chemists [AOAC] method), non-milk extrinsic sugars (NMES: total of sugars added during manufacturing or before consumption, sugars in honey, syrups and unsweetened fruit juices, and 50% of sugars from dried, stewed or canned fruit) and alcohol. Self-reported PA in the past seven days was assessed using the International Physical Activity Questionnaire (IPAQ) short version at the same time

points[15] and was used to calculate Metabolic Equivalent of Task (MET). Walking at 3.0 miles per hour is a 3.3 MET activity, and an hour of brisk walking equates to 3.3 x 60 = 198 MET-minutes.

Insulin was measured by chemiluminescent microparticle immunoassay (ARCHITECT i2000, Abbott, Illinois, USA). Glucose was measured by hexokinase/glucose-6-phosphate inter-assay dehydrogenase method and colorimetric enzyme reactions were used to measure total cholesterol, triglycerides and HDL cholesterol (all ARCHITECT c1600, Abbott, Illinois, USA). Levels were measured spectrophotometrically by an automated Olympus AU600 analyser (Olympus, Rungis, France). LDL cholesterol was calculated using the formula of Friedewald *et al*[16]. Fasting insulin and glucose were combined to calculate the insulin resistance index using the homeostasis model assessment (HOMA)[17].

Statistics

We compared data from the Tam-Prev population (age, deprivation level, BMI, waist circumference, total and HDL cholesterol, smoking, alcohol and PA habits) to a population of 1072 English women aged 33-46 years in the 2012 Health Survey for England (HSE)[18]. Indices of Deprivation 2007 Layer Super Output Area Scores were identified from participant postcodes via Geoconvert[19]. There were some methodological differences between the two data sets; waist circumferences in Tam-Prev were measured across the umbilicus whereas HSE used the midpoint between the lower rib and the upper margin of the iliac crest. PA data were collected in Tam-Prev by the IPAQ short version covering the previous seven days, and in HSE by a longer set of questions covering the previous four weeks[18]. We assessed changes in weight, BMI, body composition, waist circumference and dietary intakes at one year in the Tam-Prev cohort. Changes in lipids, glucose or HOMA were not assessed as these can be altered by tamoxifen[20,21].

Data were analysed using SPSS v23 (IBM, Armonk, New York, USA). Normally distributed data are presented as mean and SD (age, body fat percentage, waist, total, LDL and HDL cholesterol, glucose, fibre and saturated fat), otherwise median and range are presented. Categorical data are presented as number and percentage (deprivation, smoking, proportion not meeting recommendations for BMI, body fat percentage, waist, lipids, glucose, PA and dietary variables). Independent samples t-tests, Mann-Whitney U tests and Pearson's chi squared tests were used to compare the Tam-Prev and HSE populations at baseline. Changes over one year were calculated for weight, BMI, body fat, waist, PA and the dietary variables using both per protocol and baseline observation carried forward (BOCF) values. Normally distributed change variables (weight, BMI, body fat, waist, PA and saturated fat) were compared using paired samples t-tests, otherwise related samples Wilcoxon signed-rank tests were used.

Results

Baseline characteristics

Baseline characteristics of Tam-Prev participants are reported in Table 1. At the time of joining, participants had been under the care of the FHC for a median of four (range 0-19) years and none were known BRCA gene mutation carriers. The Tam-Prev population was marginally older than the HSE population but had an equivalent spread of deprivation. Women in Tam-Prev were slightly taller (mean [SD] 1.65 [0.06] vs 1.63 [0.06] cm, p<0.001), however median BMIs of the populations were comparable (median [range] 25.9 [18.4-50.8] kg/m^2 Tam-Prev and 25.8 [15.71-58.44] kg/m^2 HSE, p=803) because the Tam-Prev population were non-significantly heavier than the HSE population (median [range] 70 (45.5-130.2) vs 68.5 (37.5-140.4), p=0.106). The majority of women in both populations were either overweight or obese (59.2 and 55.3% in Tam-Prev and HSE). This aligns with the observation that half of women in Tam-Prev had a body fat percentage above the normal range[22]. The mean waist measurement of women in Tam-Prev was significantly greater than the general population (90.4 [16.0] vs 86.1 [12.7] cm, p=0.001). This is likely to be due to different measurement

techniques used in the two studies and not the small height difference. Mean total cholesterol level was lower in the Tam-Prev population compared to the general population (4.9 [0.8] vs 5.2 [1.0] mmol/L, p<0.001), however the HDL fraction was also lower (1.5 [0.3] vs 1.6 [0.4] mmol/L, p<0.001) and 26.7% of Tam-Prev women had a low HDL level (<1.29 mmol/L) compared to 17.6% of the HSE population (p=0.019), which is one of the markers of the metabolic syndrome[23]. Other markers of the metabolic syndrome were present in Tam-Prev women; 13.9% had triglycerides ≥1.7 mmol/L and 4.4% had fasting plasma glucose ≥5.6 mmol/L[23]. HOMA, a measure of insulin resistance which increases risk of metabolic syndrome, was increased (>2.5) in 14.1% of Tam-Prev women[24].

Table 1: Baseline characteristics of women in the Tam-Prev study compared to an age matched women in the general population in England

	Tam-Prev population	**English population** [1]	**P value**
Age (years) [2]	41.2 (3.5) (n=136)	39.7 (4.0) (n=1072)	**<0.001**
Indices of Deprivation [3] 1 (least deprived) 2 3 4 5 (most deprived)	 33 (24.3%) 34 (25.0%) 24 (17.6%) 25 (18.4%) 20 (14.7%) (n=136)	 234 (21.8%) 209 (19.5%) 217 (20.2%) 210 (19.6%) 202 (18.8%) (n=1072)	0.439
Height (m) [2]	1.65 (0.06) (n=130)	1.63 (0.06) (n=955)	**<0.001**
Weight (kg) [4]	70 (45.5 – 130.2) (n=130)	68.5 (37.5 – 140.4) (n=898)	0.106
BMI (kg/m^2) [4]	25.9 (18.4 – 50.8) (n=130)	25.8 (15.71 – 58.44) (n=894)	0.803
BMI category [3, 5] Underweight (<18.5 kg/m^2) Normal (18.5 – 24.9 kg/m^2) Overweight (25 – 29.9 kg/m^2) Obese (≥30.0 kg/m^2)	 1 (0.8%) 52 (40.0%) 46 (35.4%) 31 (23.8%) (n=130)	 14 (1.6%) 386 (43.2%) 279 (31.2%) 215 (24.0%) (n=894)	0.709
Body fat percentage (%) [6] **Body fat percentage over the ideal for their age** [7]	34.2 (7.3) (n=130) 50%	No data No data	- -
Waist (cm) [2, 8]	90.4 (16.0) (n=131)	86.1 (12.7) (n=659)	**0.001**
Total cholesterol (mmol/L) [2]	4.9 (0.8) (n=135)	5.2 (1.0) (n=488)	**<0.001**
LDL cholesterol (mmol/L) [6]	3.0 (0.7) (n=135)	No data	**-**
HDL cholesterol (mmol/L) [2]	1.5 (0.3) (n=135)	1.6 (0.4) (n=488)	**<0.001**

HDL cholesterol <1.29 mmol/L [3, 9]	26.7%	17.6%	**0.019**
Triglycerides (mmol/L) [10] **Triglyceride level ≥1.7 mmol/L** [9]	0.8 (0.3 – 3.1) (n=136) 13.9%	No data	-
Glucose (mmol/L) [6] **Glucose ≥5.6 mmol/L** [9]	4.7 (0.4) (n=136) 4.4%	No data	-
HOMA insulin resistance [10] **HOMA insulin resistance ≥2.5** [11]	1.5 (0.4 – 6.1) (n=135) 14.1%	No data	-

[1] [(18)], [2] Mean (SD) and independent samples t-test, [3] Percentage and Pearson's chi squared, [4] Median (range) and Mann Whitney U test, [5] [(52)], [6] Mean (SD), [7] [(22)], [8] Waist for Tam-Prev population measured across umbilicus, HSE measured at the midpoint between the lower rib and the upper margin of the iliac crest, [9] [(23)], [10] Median (range), [11] [(24)]

Table 2 compares health behaviours in the two populations. Smoking was less prevalent amongst the Tam-Prev women (10.5 vs 18.2%, p=0.032). A third of women in both populations did not meet PA guidelines. Median daily alcohol intake was markedly higher in Tam-Prev women (13.6 [0-107.8] vs 3.6 [0-680.0] g per day, p<0.001) and 45% of Tam-Prev participants exceeded the recommended UK maximum of 14 units per week(equivalent to 1.4 bottles of wine or six pints of lager) compared to 18.7% of the HSE population (p<0.001). Proportions of Tam-Prev women not meeting UK guidelines for fibre, saturated fat and NMES were 88%, 65% and 21% respectively, though there were no comparable figures for the HSE population.

Table 2: Baseline health behaviours of women in the Tam-Prev study compared to an age matched women in the general population in England

	Tam-Prev population	**English population** [1]	**P value**
Smoker [2]	10.5% (n=124)	18.2% (n=1071)	**0.032**
Do not meet physical activity guidelines [2, 3] (minimum 150 min/week moderate intensity or 75 min/week vigorous intensity physical activity or a combination)	30.6% (n=134)	35.1% (n=1059)	0.229
Alcohol intake (g per day) [4] **Exceed UK guidelines of ≤14 units per week** [2] (8g = 1 unit of alcohol)	13.6 (0 – 107.8) 45.0% (n=131)	3.6 (0 – 680.0) 18.7% (n=1049)	**<0.001** **<0.001**
Fibre (g per day) [5] **Do not meet UK daily recommendation of >24g/ day** [6]	17.5 (5.3) 87.8%	No data	-
Saturated fat (g per day) [5]	26.1 (10.3)	No data	-

Percentage of daily energy from saturated fat [5] **Exceed UK recommendation of <11% of energy** [6]	12.4 (3.1) % 64.9%		
Non-milk extrinsic sugar (g per day) [7] **Percentage of daily energy from non-milk extrinsic sugars** [5] **Exceed UK recommendation of <11% of energy** [6]	37.2 (0.1 – 145.1) 8.1 (4.6) % 21.4%	No data	-

[1] [(18)], [2] Percentage and Pearson's chi squared, [3] Physical activity data for Tam-Prev collected using IPAQ short version covering the previous seven days, HSE used a longer set of questions covering the previous four weeks, [4] Median (range) and Mann Whitney U test, [5] Mean (SD), [6] [(53)], [7] Median (range)

Of 115 women in Tam-Prev with full information, over half (51%) had at least two out of four key lifestyle risk factors for BC as defined by the World Cancer Research Fund and the American Institute for Cancer Research (overweight or obesity, low PA, smoking, exceeding seven alcoholic drinks per week: 9-13 units / week), 18% had at least three, and one patient had all four. Only 8.7% had a low-risk lifestyle with none of these risk factors[25].

Withdrawal from the Tam-Prev Study

Twenty-seven women (19.9%) withdrew before one year: 21 (15.4%) due to tamoxifen side effects, three (2.2%) lost contact, one (0.7%) became pregnant and two (1.5%) left for other reasons. There were no differences in baseline BMI or smoking status between completers and those that dropped out (median BMI [range] 26.3 [18.4-45.7] vs 25.2 [19.5-50.8] kg/m^2, p=0.943; 10.1 vs 13.3% smokers, p=0.701), however completers had a higher alcohol intake (15.6 [0.0-107.8] vs 4.0 [0.0-58.6] g/day, p=0.001). Three participants took tamoxifen for less than one year but their results are included here as they completed the one year assessments.

Change after one year of chemoprevention

Per-protocol analyses are reported in Table 3. BOCF analyses gave similar results (data not shown). There were modest reductions in weight, BMI and body fat mass over the year. Using ±3% to define natural daily weight variation[26], 23% of women lost weight, 68% maintained, and 9% gained. The proportions losing and gaining a clinically significant 5% of baseline weight were 15.7% and 4.6% respectively[27]. Neither PA nor alcohol intake changed during the year.

There were small reductions in saturated fat (26.1g to 24.0g per day, p=0.011) and NMES (37.2g to 33.7g per day, p=0.030), but no change in other dietary parameters. Despite these reductions, 65.3% and 18.8% of women exceeded recommendations at one year for saturated fat and NMES intakes respectively. Significant proportions of the women remained overweight and were not adhering to recommendations for PA, alcohol or diet at one year.

Table 3: Per-protocol analysis of change at one year

	Baseline (completers only, n=109)	One year	p value for change	% not meeting UK recommendations at baseline	% not meeting UK recommendations at one year
Weight (kg) [1] (n=108)	74.8 (17.6)	73.8 (17.1)	**0.001**	-	-
BMI (kg/m^2) [1] (n=108)	27.2 (6.0)	26.9 (5.9)	**0.001**		
BMI category [2]					
Underweight (<18.5 kg/m^2)				0.9%	0.9%
Normal (18.5 – 24.9 kg/m^2)				39.8%	43.5%
Overweight (25 – 29.9 kg/m^2)				35.2%	31.5%
Obese (≥30.0 kg/m^2)				24.1%	24.1%
Body fat (kg) [1] (n=108)	26.6 (11.7)	26.0 (11.6)	**0.010**	-	-
Waist (cm) [1] (n=108)	90.1 (15.3)	90.5 (14.8)	0.556		
Waist >80cm [3]				68.8%	74.1%
Physical activity (Metabolic Equivalent of Tasks [MET]-minutes / week) [1] (n=109)	3249 (2750)	3054 (2473)	0.719	30.3%	27.6%
Alcohol (g per day) [3] (n=101)	15.6 (0.0 – 107.8)	15.8 (0 – 91.3)	0.496	49.5%	50.5%
Fibre (g per day) [3] (n=101)	17.9 (7.0 – 34.8)	16.8 (0.9 – 41.2)	0.085	84.2%	92.3%
Saturated fat (g per day) [1] (n=101)	26.1 (10.2)	24.0 (8.4)	**0.011**	61.4%	65.3%
Non-milk extrinsic sugar (g per day) [3] (n=101)	37.2 (0.1 – 145.1)	33.7 (1.9 – 195.7)	**0.030**	20.8%	18.8%

[1] Mean (SD) for values at baseline and one year, paired samples t-test for change, [2 (52)], [3 (23,54)], [3] Median (range) for values at baseline and one year, related samples Wilcoxon signed rank test for change

Discussion

Here we report lifestyle behaviours and health measures in women in an FHC taking tamoxifen for prevention of BC, and the change in these during a year of chemoprevention. At baseline, Tam-Prev participants had a high prevalence of unhealthy lifestyle behaviours, for example overweight, larger waist, low PA and adverse health measures, which were similar to an English, age-matched female population from the HSE. They also had higher alcohol intake but lower smoking rates. Significant proportions were found to have markers of poor metabolic health and indicators of poor diet.

Previous studies of lifestyle behaviours in women at increased risk of BC in the UK have also found a high prevalence of overweight and obesity and low adherence to PA recommendations[28,29]. Begum *et al* reported the majority of women (76%) in an English FHC were overweight or obese, 24% did no PA and 78% did less than four hours PA per week[28], while Anderson *et al* found 52% of respondents in a Scottish genetics service were overweight or obese and 55% did not adhere to PA recommendations[29]. Both studies used self-reported methods for PA which are acknowledged to overestimate[30] so it is likely that actual PA levels were even lower than reported.

The lower rate of smoking in Tam-Prev (10.5%) compared to the general population (18.2%) is an interesting observation. Rouleau *et al* also found a lower prevalence of smoking in a population of women from Quebec with a family history of breast and/or ovarian cancer undergoing genetic testing[31]. Two UK surveys found many women with a family history of BC believe that smoking is one of the key risk factors[28,29] rather than weight and lack of PA which have a greater impact on risk[32]. The low rates of smoking (around 10%) seen in the surveys could be due to these beliefs.

We reported 45% of the Tam-Prev population exceeded alcohol recommendations. Similarly, the majority of women (56%) in a Scottish genetics service exceeded recommendations[29], however only 1% did in a survey of women in an English FHC[28] despite intakes being self-reported in both studies. The apparent greater alcohol intake in the Tam-Prev than HSE populations could be the result of a difference in methods; HSE used a verbal food frequency questionnaire and Tam-Prev used a seven day food diary which may provide a more honest and accurate reflection of behaviours.

Women in Tam-Prev, who all had a family history of BC, had a greater mean waist circumference compared with the general population which concurs with previous research[33,34]. However the difference reported here may be because the Tam-Prev study measured waist at the umbilicus which gives larger readings than the midpoint between the lower rib and the upper margin of the iliac crest as used in the HSE[35].

Women about to commence tamoxifen had lower levels of total and HDL cholesterol than women in the general population. Two studies by Boyd *et al* reported generally more favourable lipid profiles in women with a family history of BC, but findings were variable and the reasons for these potential differences are not understood[36,37]. Women with a family history of BC are reported to underestimate their CVD risk and overestimate their BC risk[38]. Our results suggest that a significant proportion of Tam-Prev women had an increased risk of CVD at baseline. Despite tamoxifen provoking beneficial reductions in total and LDL-cholesterol levels, it does not consistently lead to lower CVD rates, perhaps due to detrimental effects on triglyceride levels[20] and insulin sensitivity[21].

Unhealthy behaviours amongst women with a family history of BC are not confined to the UK. A study of female BRCA mutation carriers in The Netherlands reported 40.7% overweight or obese, 27.0% current smokers, 47.5% physically inactive and 3.4% drank eight or more alcoholic beverages per week. Of those with complete lifestyle data, 32.1% had a low-risk lifestyle for BC (healthy weight, achieved PA recommendations, non-smokers, consumed seven alcoholic drinks or fewer per week) compared to just 8.7% in Tam-Prev[25,39]. Bostean *et al* reported that compared to Californian women

with no family history of cancer, women with a family history did not have better overall lifestyle behaviours scores, which included BMI, diet and PA[40].

Tam-Prev participants did not receive lifestyle advice, however they completed food diaries at baseline and one year which are known to promote behaviour change[41] and could have contributed to the small improvements in weight and diet seen here. Sixteen percent of women achieved a clinically significant 5% weight loss. Our results agree with previous research showing that tamoxifen does not cause weight gain in the prevention setting[42].

The National Institute for Health and Care Excellence (NICE) recommend that women with a family history of BC in the UK receive written information on lifestyle, including diet, PA and alcohol[43] however patient surveys suggest this is not commonplace [29].

Studies have found minimal or no change in lifestyle after BRCA counselling[44–46]. This is supported by a recent meta-analysis which found that disease risk information, even when personalised, does not have a strong effect on behaviour[47]. Belief in the efficacy of certain health behaviours to prevent or delay cancer has been associated with practice of these behaviours[44]. Therefore efforts to encourage behaviour change in FHCs should include education to address current poor understanding and improve credibility of lifestyle risk factors, and their response efficacy. This should be combined with an intervention proven to aid behaviour change such as a self-monitoring website with additional telephone calls[48,49].

This is the first prospective study on lifestyle behaviours and health measures in women undertaking BC chemoprevention. It benefits from an almost complete data set for women who entered Tam-Prev. Weaknesses include the comparison of the Tam-Prev population to the general English population in the HSE. We do not have data on women in our regional FHC who opt not to take tamoxifen, therefore cannot assess differences in lifestyle risks. The absence of a control group means we are unable to assess whether the changes observed differ in populations not on chemoprevention. Dietary and PA data were self-reported and people tend to underestimate amounts eaten and overestimate PA[30,50,51]. It is recognised that this could affect both data sets, though a strength is that both studies used self-reported measures.

The prevalence of suboptimal lifestyle behaviours amongst high risk women taking chemoprevention supports the need to embed lifestyle change in FHCs. Future research should focus on engaging high risk women with lifestyle improvement. This should reduce the burden of BC and other lifestyle-related diseases, leading to potential improvements in quality of life, and cost savings for the NHS.

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Ethical approval
Tam-Prev was approved by Greater Manchester West Research Ethics Committee (11/H1014/4) and performed in accordance with the Declaration of Helsinki. All participants provided written informed consent.

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Conflict of interest statement

The authors declare no conflicts of interest.

References

1 Breast cancer incidence (invasive) statistics | Cancer Research UK. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive (accessed 12 Mar2018).

2 Parkin D. 3. Cancers attributable to consumption of alcohol in the UK in 2010. *Br J Cancer* 2011; **105**: 14–18.

3 World Cancer Research Fund International / American Institute for Cancer Research. Cancer preventability estimates. Available at wcrf.org/cancer-preventability-estimates (accessed 2 Mar2017).

4 Macacu A, Autier P, Boniol M, Boyle P. Active and passive smoking and risk of breast cancer: a meta-analysis. *Breast Cancer Res Treat* 2015; **154**: 213–224.

5 Kispert S, McHowat J. Recent insights into cigarette smoking as a lifestyle risk factor for breast cancer. *Breast cancer* 2017; **9**: 127–132.

6 Goodwin PJ. Obesity, insulin resistance and breast cancer outcomes. *Breast* 2015; **24**: S56–S59.

7 Cecchini RS, Costantino JP, Cauley JA, Cronin WM, Wickerham DL, Land SR *et al.* Body mass index and the risk for developing invasive breast cancer among high-risk women in NSABP P-1 and STAR breast cancer prevention trials. *Cancer Prev Res (Phila)* 2012; **5**: 583–92.

8 Dignam JJ, Wieand K, Johnson KA, Fisher B, Xu L, Mamounas EP. Obesity, tamoxifen use, and outcomes in women with estrogen receptor-positive early-stage breast cancer. *J Natl Cancer Inst* 2003; **95**: 1467–76.

9 Cohen I, Azaria R, Bernheim J, Shapira J, Beyth Y. Risk factors of endometrial polyps resected from postmenopausal patients with breast carcinoma treated with tamoxifen. *Cancer* 2001; **92**: 1151–1155.

10 Al-Azemi M, Labib N., Omu A. Endometrial changes in post-menopausal breast cancer patients on tamoxifen. *Int J Gynecol Obstet* 2002; **79**: 47–49.

11 Antoniou A, Pharoah PDP, Narod S, Risch HA, Eyfjord JE, Hopper JL *et al.* Average Risks of Breast and Ovarian Cancer Associated with BRCA1 or BRCA2 Mutations Detected in Case Series Unselected for Family History: A Combined Analysis of 22 Studies. *Am J Hum Genet* 2003; **72**: 1117–1130.

12 Donnelly LS, Evans DG, Wiseman J, Fox J, Greenhalgh R, Affen J *et al.* Uptake of tamoxifen in consecutive premenopausal women under surveillance in a high-risk breast cancer clinic. *Br J Cancer* 2014; **110**: 1681–1687.

13 Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med* 2004; **23**: 1111–1130.

14 Harvie M, Wright C, Pegington M, McMullan D, Mitchell E, Martin B *et al.* The effect of intermittent energy and carbohydrate restriction v. daily energy restriction on weight loss and metabolic disease risk markers in overweight women. *Br J Nutr* 2013; **110**: 1534–1547.

15 Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE *et al.* International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003; **35**: 1381–95.

16 Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; **18**: 499–502.

17 Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis

model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; **28**: 412–9.
18 Craig R, Mindell J (eds). Health Survey for England 2012: Health, social care and lifestyles. Volume 1: Health, social care and lifestyles. Volume 2: Methods and documentation. Health and Social Care Information Centre, Leeds, 2013.
19 UK Data Service Census Support. Office for National Statistics, Postcode Directories [computer file]. http://edina.ac.uk/census / http://geoconvert.ukdataservice.ac.uk (accessed 30 Nov2016).
20 Filippatos TD, Liberopoulos EN, Pavlidis N, Elisaf MS, Mikhailidis DP. Effects of hormonal treatment on lipids in patients with cancer. *Cancer Treat Rev* 2009; **35**: 175–184.
21 Johansson H, Gandini S, Guerrieri-Gonzaga A, Iodice S, Ruscica M, Bonanni B *et al.* Effect of Fenretinide and Low-Dose Tamoxifen on Insulin Sensitivity in Premenopausal Women at High Risk for Breast Cancer. *Cancer Res* 2008; **68**: 9512–8.
22 Gallagher D, Heymsfield SB, Heo M, Jebb SA, Murgatroyd PR, Sakamoto Y. Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. *Am J Clin Nutr* 2000; **72**: 694–701.
23 International Diabetes Federation. IDF Consensus Worldwide Definition of the Metabolic Syndrome. Brussels, Belgium, 2006.
24 Kuk JL, Ardern CI. Are metabolically normal but obese individuals at lower risk for all-cause mortality? *Diabetes Care* 2009; **32**: 2297–9.
25 World Cancer Research Fund International / American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective.* AICR, Washington DC, 2007 doi:978-0-9722522-2-5.
26 Stevens J, Truesdale K, Mcclain J, Cai J. The definition of weight maintenance. *Int J Obes* 2006; **30**: 391–399.
27 Jensen MD, Ryan DH, Donato KA, Apovian CM, Ard JD, Comuzzie AG *et al.* Executive summary: Guidelines (2013) for the management of overweight and obesity in adults. *Obesity* 2014; **22**: S5–S39.
28 Begum P, Richardson CE, Carmichael AR, Lahmann P, Hoffmann K, Allen N *et al.* Obesity in post menopausal women with a family history of breast cancer: prevalence and risk awareness. *Int Semin Surg Oncol* 2009; **6**: 1.
29 Anderson AS, Caswell S, Macleod M, Steele RJ, Berg J, Dunlop J *et al.* Health Behaviors and their Relationship with Disease Control in People Attending Genetic Clinics with a Family History of Breast or Colorectal Cancer. *J Genet Couns* 2017; **26**: 40–51.
30 Boon RM, Hamlin MJ, Steel GD, Ross JJ. Validation of the New Zealand Physical Activity Questionnaire (NZPAQ-LF) and the International Physical Activity Questionnaire (IPAQ-LF) with accelerometry. *Br J Sports Med* 2010; **44**: 741–6.
31 Rouleau I, Chiquette J, Plante M, Simard J, Dorval M. Changes in Health-Related Behaviours Following BRCA 1/2 Genetic Testing: The Case of Hormone Replacement Therapy. *J Obstet Gynaecol Canada* 2004; **26**: 1059–1066.
32 Harvie M, Howell A, Evans DG. Can Diet and Lifestyle Prevent Breast Cancer: What Is the Evidence? *Am Soc Clin Oncol Educ B* 2015; **35**: e66–e73.
33 Harvie MN, Bokhari S, Shenton A, Ashcroft L, Evans G, Swindell R *et al.* Adult weight gain and central obesity in women with and without a family history of breast cancer: A case control study. *Fam Cancer* 2007; **6**: 287–294.
34 Dettenborn L, James GD, Britton JA, Bovbjerg DH. Higher levels of central adiposity in healthy premenopausal women with family histories of premenopausal breast cancer. *Am J Hum Biol* 2008; **20**: 355–8.
35 Mason C, Katzmarzyk PT. Variability in waist circumference measurements according to anatomic measurement site. *Obesity* 2009; **17**: 1789–1795.
36 Boyd NF, McGuire V, Fishell E, Kuriov V, Lockwood G, Tritchler D. Plasma lipids in

premenopausal women with mammographic dysplasia. *Br J Cancer* 1989; **59**: 766–771.
37 Boyd NF, Connelly P, Lynch H, Knaus M, Michal S, Fili M *et al.* Plasma Lipids, Lipoproteins, and Familial Breast Cancer. *Cancer Epidemiol Biomarkers Prev* 1995; **4**: 117–122.
38 Erblich J, Bovbjerg DH, Norman C, Valdimarsdottir HB, Montgomery GH. It won't happen to me: Lower perception of heart disease risk among women with family histories of breast cancer. *Prev Med (Baltim)* 2000; **31**: 714–721.
39 van Erkelens A, Derks L, Sie AS, Egbers L, Woldringh G, Prins JB *et al.* Lifestyle Risk Factors for Breast Cancer in BRCA1/2-Mutation Carriers Around Childbearing Age. *J Genet Couns* 2017; **26**: 785–791.
40 Bostean G, Crespi CM, McCarthy WJ. Associations among family history of cancer, cancer screening and lifestyle behaviors: a population-based study. *Cancer Causes Control* 2013; **24**: 1491–1503.
41 Burke LE, Wang J, Sevick MA. Self-Monitoring in Weight Loss: A Systematic Review of the Literature. *J Am Diet Assoc* 2011; **111**: 92–102.
42 Sestak I, Harvie M, Howell A, Forbes JF, Dowsett M, Cuzick J. Weight change associated with anastrozole and tamoxifen treatment in postmenopausal women with or at high risk of developing breast cancer. *Breast Cancer Res Treat* 2012; **134**: 727–734.
43 NICE. Clinical guideline CG164. Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer. National Institute for Health and Care Excellence, 2013https://www.nice.org.uk/guidance/cg164/chapter/1-Recommendations (accessed 17 Nov2016).
44 Quach J, Porter K, Leventhal H, Kelly KM. Health behaviors among Ashkenazi Jewish individuals receiving counseling for BRCA1 and BRCA2 mutations. *Fam Cancer* 2009; **8**: 241–250.
45 O'Neill SC, Kaufman E, DeMarco T, Peshkin BN, McKenna K, Shelby R *et al.* Changes in diet and physical activity following BRCA1/2 testing. *J Psychosoc Oncol* 2008; **26**: 63–80.
46 Spector D, Mishel M, Skinner CS, Deroo LA, Vanriper M, Sandler DP. Breast cancer risk perception and lifestyle behaviors among White and Black women with a family history of the disease. *Cancer Nurs* 2009; **32**: 299–308.
47 French DP, Cameron E, Benton JS, Deaton C, Harvie M. Can Communicating Personalised Disease Risk Promote Healthy Behaviour Change? A Systematic Review of Systematic Reviews. *Ann Behav Med* 2017; **51**: 718–729.
48 Cadmus-Bertram L, Wang JB, Patterson RE, Newman VA, Parker BA, Pierce JP. Web-based self-monitoring for weight loss among overweight/obese women at increased risk for breast cancer: the HELP pilot study. *Psychooncology* 2013; **22**: 1821–1828.
49 Hartman SJ, Dunsiger SI, Marinac CR, Marcus BH, Rosen RK, Gans KM. Internet-based physical activity intervention for women with a family history of breast cancer. *Heal Psychol* 2015; **34**: 1296–1304.
50 Mertz W, Tsui JC, Judd JT, Reiser S, Hallfrisch J, Morris ER *et al.* What are people really eating? The relation between energy intake derived from estimated diet records and intake determined to maintain body weight. *Am J Clin Nutr* 1991; **54**: 291–5.
51 Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E *et al.* Discrepancy between Self-Reported and Actual Caloric Intake and Exercise in Obese Subjects. *N Engl J Med* 1992; **327**: 1893–1898.
52 WHO. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ. Tech. Rep. Ser. 1995; **854**: 1–452.
53 Department of Health. Dietary reference values for food energy and nutrients for the United Kingdom. Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy. 1991http://www.ncbi.nlm.nih.gov/pubmed/1961974 (accessed 15 Dec2016).

54 NICE. Clinical guideline CG189. Obesity: identification, assessment and management. National Institute for Health and Care Excellence, 2014https://www.nice.org.uk/guidance/cg189/ifp/chapter/obesity-and-being-overweight (accessed 23 Nov2016).